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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
04/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/031,949	COUARAZE ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6 and 8-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6 and 8-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/27/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed on September 11, 2008. Claims 3-6 and 8-18 are pending in the application. Claims 3-6 and 8-18 will presently be examined to the extent they read on the elected subject matter of record.

Information Disclosure Statement

Information Disclosure Statement filed October 27, 2008 is acknowledged.

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhutani (US 4,684,516).

Bhutani discloses the active ingredient is first coated onto non-pareil beads (neutral microgranules, 62.5% to 91.5% sucrose and the remainder starch) or onto drug crystals or granules. Bhutani discloses these pellets are then divided into several

groups and varying amounts of retarding materials are applied to different groups. Bhutani discloses the stabilized pellets are then coated with several layers of disintegrating agent or agents (active agents) and compressed into tablets or pills, after adding a small amount of lubricants or other inert ingredients, if necessary (lubricant of 0 and 1%) (tableting premix). Bhutani discloses that such a compressed tablet, when tested in water or gastric fluid, breaks up quickly thereby releasing the individual pellets in a matter of minutes, whereupon they act as independent pellets releasing their medicine at a predetermined rate (col. 4, lines 11-29). Bhutani teaches the tablet composed of 85% to 98% of the drug-containing, coated, spherical pellets, the remainder being composed of binder and lubricants, preferably between 90% to 100% of the tablet (99 and 100% neutral microgranules). The pellets are predominantly of a size ranging from 12 to 30 mesh, with sizes 16 thru 24 mesh being preferred and they all may be the same size or of different sizes within that range (col. 5, lines 40-47). The 12 to 30 mesh is within the same range as 200 and 400 μm of the instant invention. Bhutani discloses in examples 1, 3, and 4 preparation of tablets using Nonpareil seeds (sugar pellets). Bhutani disclosed in example No. 4, Nonpareil seed (sugar pellets), 30.0 kg., all passing through a No. 30 U.S. mesh screen, 90% passing through a No. 35 U.S. mesh screen, and not over 10% passing through a No. 40 U.S. mesh screen are placed in a 48-inch coating pan. The pan is set in rotation and coating solution is sprayed slowly onto the pellets in order to wet them evenly. Then 400 gm of theophylline anhydrous containing approximately 5% talcum powder is sprinkled on the wetted mass of nonpareil seeds.

These tablets are then coated using conventional coating techniques for improving appearance and acceptability. The coated tablets thus obtained released the active ingredient at a sustained rate over a period of 10 to 12 hours under physiological conditions (col. 11, lines 1-49).

Bhutani meets all the limitations of the claims and thereby anticipates the claims.

Claims 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Harrison et al. (US 4,806,361).

Harrison et al. disclose in col. 6, lines 29-47, the preparation of Nonpareils Coated with Medicament. Harrison et al. disclose that 11 parts of hydroxypropylmethylcellulose were suspended in 111 parts of purified water previously heated to boiling. 440 additional parts of water were then added to the suspension and the whole stirred until a diluted Pharmacoat suspension had formed. Harrison et al. further disclose that 11 parts of 1,2 dihydro-3-cyano-6-methyl-5-(4-pyridinyl)-2(1H)-pyridinone (active agent) were stirred into the Pharmacoat suspension until well dispersed. 200 parts of nonpareils (sugar/starch base: 25-30 mesh) (neutral microgranules) were placed in a coating column or pan and, whilst passing an atomizing current of warm air there through, the diluted Pharmacoat suspension was gradually added. Harrison et al disclose that after all the Pharmacoat suspension had been added, the passage of the current of warm air was continued until the coated nonpareils were dry.

Harrison et al. meet all the limitations of the claims and thereby anticipate the claims.

Claims 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Hsiao (US 4,634,587).

Hsiao discloses a sustained release quinidine dosage form which comprises a plurality of pellets having an average diameter greater than about 1 mm. Each pellet has a coating of a quinidine over nonpareil seed (microneutrals coated with active agent). The quinidine-coated nonpareils are then coated with a mixture of about one and one half to about nine parts by weight ethylcellulose to about one part by weight hydroxypropylcellulose. Each pellet is coated to about 5-15% of its weight with that coating mixture. Hsiao discloses in one embodiment, the present invention provides a sustained release quinidine dosage form, as a capsule containing from about 200 to about 600 of the polymer-coated pellets. Hsiao discloses in another embodiment, pellets are compressed to a tablet. Hsiao discloses the nonpareils, typically sugar seeds having a mesh size of about 20 to about 25, are coated with more than an equal amount by weight of a quinidine compound, which preferably is quinidine bisulfate. In a preferred embodiment, about two parts by weight quinidine bisulfate are coated onto one part by weight of nonpareil seeds (col. 1, lines 13-30).

Hsiao meets all the limitations of the claims and thereby anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-6 and 8-17 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Barry (US 2,996,431) in view of Makino et al. (US 5,026,560).

Applicant's Invention

Applicant claims a tablet comprising less than 40 mg/g of active principle attached as a coating to neutral microgranules comprising 62.5 to 91.5 % sucrose and the remainder starch. Applicant claims the tablet includes a compression excipient at less than 1% by weight of the tablet.

Determination of the scope of the content of the prior art
(MPEP 2141.01)

Barry teaches a tablet which is composed essentially of two parts, a matrix or binder, and a quantity of small pellets distributed therein. Barry teaches the size, quantity and hardness of the pellet is subjected to the pressure of the thumb, accompanied by a slight turning or twisting movement (col. 1, lines 28-36). Barry teaches a medicinal agent can be contained either in the matrix, but preferably on a relatively large number of pellets distributed therein. Barry teaches the tablet should be composed of about 30 to 70% by weight of the spheroidal pellets, the remainder being composed of the matrix or binder (col. 2, lines 49-52). Barry teaches the pellets range in size from 10 to 16 mesh, sizes passing through a 12 to 14 mesh screen being preferred (col. 2, lines 60-63). Barry teaches the spheroidal pellets can be of the type commonly known in the confectionery trade as nonpareil seeds. Barry teaches these are composed of about 65 parts cane sugar, and 35 parts corn starch (col. 3, lines 4-7) (62.5 to 91.5% sucrose, remainder starch). Barry teaches a tablet composed of a large number of small pellets embedded in a matrix or binder is provided with a medicinal agent coated on the pellets in such a manner that a prolonged or sustained action is obtained (col. 3, lines 15-20). Barry teaches the pellets alone or the matrix alone, or both may serve as carrier for a medicinal agent; and different and even mutually incompatible medicinal agents can be carried by the pellets and matrix, or by different groups of pellets. Barry teaches one satisfactory form of tablet the matrix of each tablet contains a mixture of about 3.5 gr of aspirin, 2.5 g of acetophenetidin and 2 mg of 1-parachloropheny-1-(2-pyridyl-3-dimethyl-aminopropane maleate (col. 5, lines 25-34).

Barry teaches in claim 13, a pressed medicinal tablet comprising a pressure-molded matrix having embedded therein a quantity of discrete, hard, uncrushed, spheroidal pellets wherein the matrix being disintegradable by pressure of a thumb.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Barry does not teach the compression force between 10 and 30 kN or the disintegration is less than 15 minutes. It is for this reason Makino et al. is joined as a secondary reference.

Makino et al. teaches spherical granules having a core coated with spraying powder containing a drug and low substituted hydroxypropylcellulose, because of their excellent hardness, can be coated further evenly, (e.g. sustained release coating, gastric coating, enteric coating), and at the time the granules are excellent in disintegration(Abstract). Makino et al. teach seed cores include Nonpareil produced by coating sucrose (75 weight parts) with corn starch (25 weight parts) according to the per se known method, and spherical seed cores using crystalline cellulose. Makino teaches the particle size of the said seed cores is generally 14-80 mesh (col. 3, lines 30-35). Makino et al. teach the spherical granules having a core may be coated according to the per se known method for the purpose of taste masking, enteric coating, gastric coating, or prolongation, (col. 4, lines 15-19) (film coating). Experimental example 1 in col. 8, lines 20-50, teach the disintegration times and hardness of the various excipients used in the production of the granules. The disintegration ranges from 1 minute to 30 minutes.

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Barry and Makino et al. and produce tablets that have a disintegration rate less than 15 minutes. One skilled in the art at the time the invention was made would have been motivated to have a disintegration rate less than 15 minutes because Barry teaches the tablet compositions can be made by methods known in the art and that the tablets are disintegrated with the pressure of a thumb. In addition, Makino et al. teach the use of certain excipients and binders, some of which are the same binders that may be incorporated in the matrix taught by Barry, are formulated with the granules have disintegration times ranging from 1 to 30 minutes, the median of which is 15 minutes.

Each of the references is silent as to the compression force ranging between 10 and 30 kN. However the adjustment of the compression force is a matter of routine experimentation and optimization to produce the tablets. One skilled in the art at the time the invention was made would have been motivated to adjust the compression force to range between 10 and 30 kN to produce a tablet with good hardness. The adjustment of particular conventional working conditions (e.g., compression force) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. Accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited references.

Claims 3-6 and 8-17 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Frost et al. (WO 88/02629) in view of Makino et al. (US 4,983, 399).

Applicant's Invention

Applicant claims a tablet comprising less than 40 mg/g of active principle attached as a coating to neutral microgranules comprising 62.5 to 91.5 % sucrose and the remainder starch. Applicant claims the tablet includes a compression excipient at less than 1% by weight of the tablet.

Determination of the scope of the content of the prior art (MPEP 2141.01)

Frost et al. (WO 88/02629) teach on page 4, example II, alcohol dissolved Killodone 90 is used as a wetting agent for nonpareil seeds (20 to 30 mesh) in a coating pan with repeated dustings of 2', 3'-didesoxyadenosine (about ten to twenty times) to build up a 2', 3'-didesoxyadenosine-coated nonpareil seed. Frost et al. teach a total adult daily dosage is spread out over three to five administrations per day, or twice daily in the sustained release. Frost et al. teach the tablets comprise from about 2 to about 1000 mg per day, most preferably 10 to 250 mg per administration (page 4, lines 13-18) (40 mg/g active). Frost et al. teach in one embodiment there is a sustained release composition which comprises a plurality of dosage units each having at least two

components including 2', 3'-didesoxyadenosine and an outer inert component stable in acidic pH which dissolves in a basic pH. Frost et al. teach tablets of a total weight of 330 mg are produced by mixing and then compressing together in a ratio of 10:1 of the dosage subunits of example II and hydroxypropylmethyl cellulose. Frost et al. teach the sustained release tablet of example VII provides an advantage over the other dosage forms in that the dosage subunits are only gradually exposed to the environment of the gastrointestinal fluids, whereby 2',3'-didesoxyadenosine is introduced into the bloodstream over a prolonged period of time (page 6, lines 3-12). Frost et al. teach the compressed tablet containing the plurality of dosage subunits, the matrix of the tablet disintegrating in the gastrointestinal tract to yield the plurality of dosage subunits (page 2, lines 11-15).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Frost et al. do not teach the compression force between 10 and 30 kN or the disintegration is less than 15 minutes. It is for this reason Makino et al. is joined as a secondary reference.

The teachings of Makino et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Frost et al. and Makino et al. and produce tablets that have a disintegration rate less than 15 minutes. One skilled in the art at the time the

invention was made would have been motivated to have a disintegration rate less than 15 minutes because Frost et al. teach granules disintegrate rapidly in the gastrointestinal fluids. In addition, Makino et al. teach that use certain excipients and binders, some of which are the same binders that may be incorporated in the matrix taught by Barry, are formulated with the granules have disintegration times ranging from 1 to 30 minutes, the median of which is 15 minutes.

Each of the references is silent as to the compression force ranging between 10 and 30 kN. However the adjustment of the compression force is a matter of routine experimentation and optimization to produce the tablets. One skilled in the art at the time the invention was made would have been motivated to adjust the compression force to range between 10 and 30 kN to produce a tablet with good hardness. The adjustment of particular conventional working conditions (e.g., compression force) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. Accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited references.

None of the claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571)272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/John Pak/
Primary Examiner, Art Unit 1616